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CASE REPORT | COLON

Colitis Following Initiation of Sofosbuvir and Simeprevir for Genotype 1 Hepatitis C

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Abstract

Sofosbuvir and simeprevir are used for the treatment of chronic hepatitis C (HCV) genotype 1. Both drugs have been well-tolerated, with diarrhea noted in 6% cases with sofosbuvir, 16% with sofosbuvir plus simeprevir, and 0% with simeprevir. No prior reports exist of colitis secondary to either drug or their combination. We report a patient with no prior history of inflammatory bowel disease who developed significant bloody diarrhea within 2 weeks of sofosbuvir/simeprevir initiation. Colonoscopy and biopsy confirmed pancolitis, which responded to mesalamine and completion of sofosbuvir/simeprevir.

Introduction

Hepatitis C virus (HCV) infection poses a significant public health challenge with substantial morbidity and mortality. New interferon-free therapies have excellent sustained virologic response rates (SVRs; >90%) with minimal side effects.[1,2] The U.S. Food and Drug Administration recently approved the combination of sofosbuvir, a NS5B polymerase inhibitor, and simeprevir, a NS3 protease inhibitor, for the treatment of chronic HCV genotype 1. Sofosbuvir and simeprevir have been well-tolerated, with diarrhea noted in 6% cases with sofosbuvir, 16% cases with sofosbuvir/simeprevir, and 0% with simeprevir.[1-3] No prior reports of colitis or exacerbation of chronic colitis secondary to either drug or their combination exist in MEDLINE, EMBASE, or post-marketing safety records.

Case Report

A 50-year-old Hispanic man with HCV genotype 1 and well-compensated cirrhosis was evaluated for retreatment of HCV. He was a responder/relapser to telaprevir, pegylated interferon, and ribavirin, but otherwise had an unremarkable medical history. He was a non-smoker with remote history of alcohol use, unremarkable family history, no known allergies, and was not taking any prescribed medications or supplements. He was interferon-ineligible due to thrombocytopenia, and started treatment with sofosbuvir 400 mg and simeprevir 150 mg daily. After 2 weeks of treatment, he noted increased flatulence and loose stool with intermittent blood. This was presumed to be self-limited, and a possible side effect of sofosbuvir/simeprevir, but worsened over the following 2 weeks. Stool studies for *Clostridium difficile*, bacterial culture, and ova and parasites were negative. Serum albumin was 4 g/dL, and electrolytes, blood panel, and coagulation laboratory tests were normal, except for low platelets at baseline. He underwent sigmoidoscopy, which revealed erythematous friable mucosa without skip areas, with chronic active colitis on biopsy (Figure 1).

Sofosbuvir/simeprevir was continued, but given persistent bloody diarrhea, he underwent colonoscopy at week 9 of therapy. This showed persistent, mild to moderate chronic colitis (Figure 2). Terminal ileum was unremarkable both

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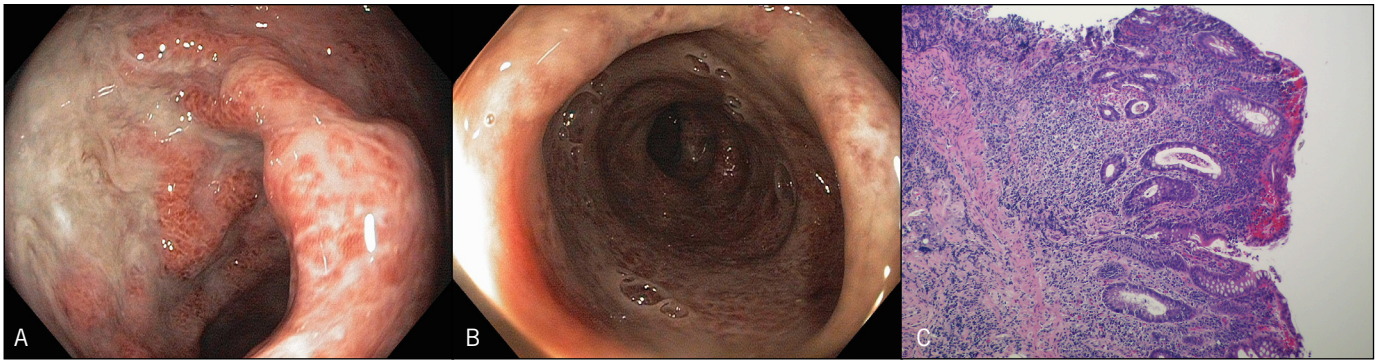

Figure 1. Endoscopic and microscopic images of the colon indicative of chronic active colitis at week 4 of sofosbuvir/simeprevir therapy. (A, B) Erythematous friable mucosa with exudates without skip areas. (C) Marked increase in lamina propria lymphoplasmacytic inflammatory infiltrate, significant basal lymphoplasmacytosis with reactive lymphoid aggregates, mucosal distortion, lamina propria neutrophils, acute cryptitis, crypt abscesses, and surface damage suggestive of erosions.

endoscopically and histologically. On week 10 of therapy, he was initiated on 2.4 g mesalamine once daily, with resolution of his diarrhea over the following 2 weeks. He remained clinically asymptomatic on mesalamine, and achieved SVR. Seven months after completion of sofosbuvir/simeprevir treatment, but with the patient still taking mesalamine, repeat colonoscopy demonstrated normal mucosa macroscopically with minimal inflammatory changes on colonic mucosa and focal minimal non-specific ileitis (Figure 3). Serologic and genetic testing was performed using the PROMETHEUS® IBD sgi Diagnostic™ test (Prometheus Laboratories, Inc., San Diego, CA). The results revealed a possible predisposition to IBD, specifically Crohn's disease.

Discussion

Neither drug-induced colitis nor the development of chronic colitis triggered by sofosbuvir, simeprevir, or sofosbuvir/simeprevir has been previously described. Testing of our patient would suggest genetic predisposition for IBD, and we hypothesize that colitis may have been triggered on initiation of sofosbuvir and/or simeprevir.[4] A wide variety of drugs have been implicated in drug-induced colitis presenting with a heterogeneous array of clinical, endoscopic, and pathologic findings without a clear understanding of the pathophysiologic mechanism.[5] Drug-induced colitis is sometimes difficult to discern from other etiologies of colitis. Our patient had mild to moderate symptoms and responded very well to mesalamine, allowing completion of sofosbuvir/simeprevir. As sofosbuvir and sofosbuvir/simeprevir regimens are used more frequently, more cases of diarrhea may be reported. Patients with persistent or bloody diarrhea post-initiation of sofosbuvir- and/or simeprevir-based regimens should be adequately investigated for IBD-like colitis and managed appropriately.

Disclosures

Author contributions: S. Sarkar and S. Jakab researched and wrote the manuscript. KA Mitchell contributed to the pathology, writing, and discussion. JK Lim and I. Oikonomou wrote the manuscript. S. Jakab is the article guarantor.

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Informed consent was obtained for this case report.

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Figure 2. Endoscopic and microscopic images of the colon at week 9 of sofosbuvir/simeprevir. (A, B) Mild erythema in the cecum, with moderate erythema friability with few exudates in the rectosigmoid colon and loss of vascular pattern. (C) Crypt destruction with mucosal erosion-active colitis.

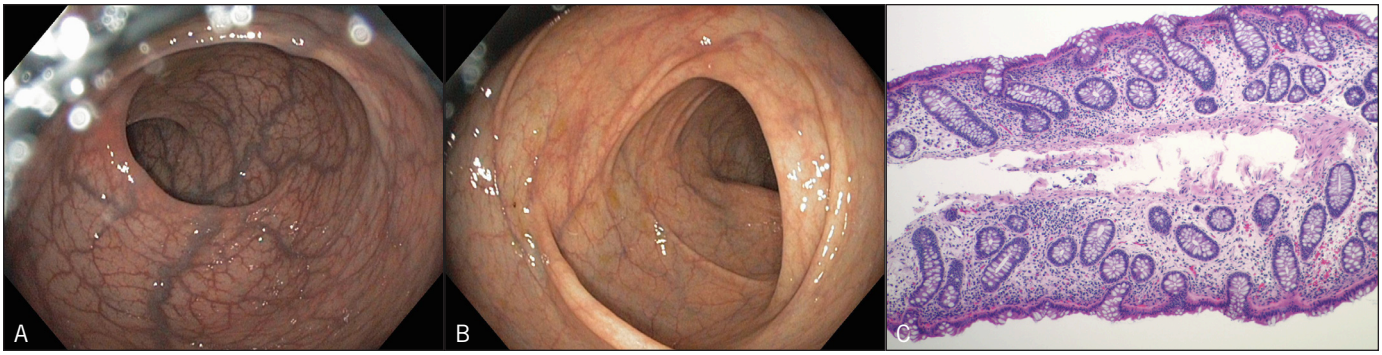

Figure 3. Endoscopic and microscopic images of the colon 28 weeks after completion of sofosbuvir/simeprevir. (A, B) Normal mucosa. (C) Reactive colonic mucosa with minimal inflammatory changes.

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